PREGNANCY PEARLS
FOR THE INTERNIST

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IT’S ON OUR BOARDS!

OBJECTIVES

- Physiologic changes in pregnancy
- FDA classification system & Drugs contraindicated in pregnancy
- Common medical illnesses in pregnancy

Adapting to Support Another Life…

INCREASED

- Plasma volume 50%
- RBC volume 20%
- CO 130-150%
- HR by 10 bpm
- GFR
- Insulin Resistance
- Tidal Volume

DECREASED

- SVR
- SBP & DBP
- BUN and Cr
- FRC and RV late in pregnancy

FIRST TRIMESTER USE OF PRESCRIPTION DRUGS

Drug Class	Percentage
Antibiotics	35.3
Antihistamines	27.3
Misc Gastrointestinal	14.7
Hormonal Agents	11.4
Nonnarcotic Analgesics	10.8
Narcotic Analgesics	8.1

Little BB, Gilstrap LC III: Human Teratology Principles. In Gilstrap LC III, Little BB (eds): Drugs and Pregnancy. New York, Elsevier, 1992, p3.

FDA PREGNANCY RISK CATEGORIES

- **A:** Controlled human studies with no risk to fetus
- **B:** Animal studies without adverse affects but no controlled human studies, OR animal studies revealed some adverse affects but human studies have not
- **C:** Either animal studies with adverse affect but no human studies, OR no animal or human studies.
- **D:** Evidence of human fetal adverse affects, however, benefit may still outweigh risk.
- **X:** Demonstrable human fetal risk that clearly outweighs any potential benefit (teratogens).

DRUGS CONTRAINDICATED IN PREGNANCY

- Aminopterin & Methylaminopterin
- Androgenic hormones
- Busulfan
- Coumadin
- Cyclophosphamide
- Diethylstilbestrol
- Etretinate
- Isotretinoin
- Lithium
- Methimazole
- Penicillamine
- Phenytoin
- Tetracyclines
- Thalidomide
- Trimethadione
- Valproic Acid

Little BB, Gilstrap LC III: Human Teratology Principles. In Gilstrap LC III, Little BB (eds): Drugs and Pregnancy. New York, Elsevier, 1992, p9.

MOST ASKED ABOUT DRUGS IN PREGNANCY

DRUGS TO AVOID

- Valproic acid, trimethadione
- ACE Inhibitors
- Ciprofloxacin
- Podophyllin
- Methimazole
- I-131
- Most antihistamines
- Warfarin
- Nitroprusside
- Most aminoglycosides
- Doxycycline, TCN
- Metronidazole in 1st trimester

RELATIVELY SAFE

- Prednisone
- Heparin
- Sulfasalazine
- Digoxin, verapamil, procainamide, cardioversion
- Clonidine, labetalol, Ca blockers
- PTU
- Chlorpheniramine
- Gentamicin
- Betalactams
- Amphotericin B

Medstudy

HYPERTENSION

- 6-8% of all pregnancies
- 15% of all maternal deaths
- Categories:
  1. Chronic essential HTN
  2. Pregnancy induced HTN (preeclampsia)
  3. Chronic renal disease
  4. Gestational HTN

CHRONIC ESSENTIAL HYPERTENSION

- Prior to 20 weeks gestation
- Rule out secondary causes: (hyperaldosteronism, pheochromocytoma, renal disease)
- Bottom line: Treat!
  - Aldomet B
  - Hydralazine C
  - Beta Blockers C
  - Clonidine C
  - Ca Antagonists C
- AVOID ACE Inhibitors: Increased fetal loss and renal tubular dysplasia and Nitroprusside: Cyanide poisoning

PREECLAMPSIA

- 5-22% of pregnancies - etiology unknown
- 3rd trimester
- HTN, edema, proteinuria, seizures (eclampsia)
- Signs/Sxs: Hyperactive DTRs, fundoscopic changes, rales, headache, anxiety, epigastric pain
- Labs: Increased uric acid (decreased GFR)
- Risk Factors: Nulliparity, DM, APA, HTN, mult gestation, fam hx, renal dz, BP > 160/100, retinal hemorrhage, Inc LFTs, low plts, MAHA
- Prevention: Low dose aspirin (>100mg)
- Treatment: Delivery!!

CLINICAL FEATURES OF HYPERTENSIVE DISORDERS IN PREGNANCY

FEATURE	ESSENTIAL HTN		RENAL DISEASE		PRE-ECLAMPSIA	
	1ST HALF	2ND HALF	1ST HALF	2ND HALF	1ST HALF	2ND HALF
Hypertension	+/-	+	+/-	+	-	+
Proteinuria	-	-	+	+	-	+
Microscopic Hematuria	-	-	+/-	+/-	-	-
Incr. Creatinine (≥1.0)	-	-	+/-	+/-	-	+/-
Incr. Uric Acid (≥4)	-	-	-	-	-	+
Coag Abnormalities	-	-	-	-	-	+/-

Paller, MS: Disease of the Month: Hypertension in Pregnancy. J Am Soc of Nephrolo

OTHER CARDIOVASCULAR COMPLICATIONS

- Arrhythmias
- Valvular Heart Disease: Mitral stenosis
  - A fib/pulmonary edema
  - Digoxin
  - Porcine valve
- Ischemic Heart Disease
  - 1 in 10,000
  - Advanced maternal age, DM, cocaine

ASTHMA

- 4% of pregnancies
- Effects of pregnancy on asthma:
  - Rule of 1/3's
  - GERD major trigger
- Effects of uncontrolled asthma on pregnancy:
  - increased incidence of preeclampsia, gestational HTN, hyperemesis gravidarum, vaginal hemorrhage, IUGR, preterm birth, neonatal hypoxia, perinatal death

ASTHMA: TREATMENT

- Avoid triggers and treat aggressively!
- Stepwise therapy
  - mild intermittent: Beta-agonist
  - Cromolyn sodium
  - Inhaled corticosteroid (Beclomethasone)
  - Early systemic steroids
  - Theophylline for nocturnal asthma
  - Leukotriene antagonists
- Follow PFTs and Peak flows

ALLERGIC RHINITIS

- Antihistamines:
  - Fexofenadine (Allegra) C
  - Cetirizine (Zyrtec) B
  - Loratidine (Claritin) B
  - Chlorpheniramine (Chlor-trimeton) B *
- Decongestants:
  - pseudoephedrine (sudafed) C

ANTIBIOTICS

- Penicillins and Cephalosporins B
- Macrolides B
  - expect same side effects as nonpregnant state
  - Clarithromycin (Biaxin) C
- Clindamycin
- AVOID: tetracyclines, fluoroquinolones, metronidazole, sulfa close to term

DIABETES

- Gestational, Type I, and Type II
- “White’s Classification”
  - **A1**: Normal fasting in gestational DM
  - **A2**: Abnormal fasting in gestational DM
  - **B**: Diabetes onset after 20yo; duration < 10yrs
  - **C**: Diabetes onset before 20yo; duration > 10yrs
  - **D**: Diabetes onset b/w 10-19yo; duration 10-19yrs
  - **F**: Presence of nephropathy
  - **R**: Presence of proliferative retinopathy
  - **H**: Presence of arteriosclerotic heart disease

Sakala, Elmar P. Obstetrics and Gynecology. Williams & Wilkins, 1997, p11

TYPE I AND TYPE II DIABETES

- Increased risk:
  - Spontaneous abortions, stillbirths
  - IUGR
  - Neural tube defects
  - Congenital malformations
  - Macrosomia/shoulder dystocia/increased C-sections
  - Neonatal hypoglycemia, hypocalcemia, hyperbilirubinemia
- Optimal glycemic control prior to conception and during pregnancy
- Increased insulin requirements due to diabetogenic state

THE THYROID

	Normal Pregnancy	Hyperthyroidism
TSH	-	Decreased
TBG	Increased	-
Total T4	Increased	Increased
Free T4	-	Increased
Total T3	Increased	Increased
Free T3	-	Increased
T3RU	Decreased	Increased

Gordon, JD, Rydfors, JT, Druzin, ML, and Tadir Y. Obstetrics Gynecology & Infertility. Scrub Hill Press, INC. NY 1997. p67

TREATMENT

- Hypothyroidism
  - Synthroid
  - Follow TSH as requirements may increase
- Hyperthyroidism
  - Propylthiouracil (PTU)
  - AVOID: Methimazole (neonatal aplasia cutis) and I131
  - All can cause neonatal hypothyroidism or goiter

GASTROENTEROLOGY

- GERD: Increased incidence
- Biliary Disease:
  - Increased biliary secretion of cholesterol
  - Cholecystectomy 2nd most common non-gyn surgery in pregnancy
    - treat during 1st trimester with ursodiol; elective surgery during 2nd trimester)
- Acute Fatty Liver of Pregnancy:
  - microvesicular

HEPATITIS IN PREGNANCY

- Hepatitis E - Increased mortality 20-30%
- Hepatitis B:
  - Course of infection unaltered during pregnancy
  - Fetal infection greatest when mother contracts in 3rd trimester
  - HepBeAg determinant of maternal-fetal transmission
  - Administer HepB immune globulin and vaccine w/in 48 hrs after birth
  - Chronic active hepatitis: Incr. Premature births, low birth weight, neonatal death
  - Vaccine safe to give

SYSTEMIC LUPUS ERYTHEMATOSUS

- Increased 2nd trimester loss, PPROM, preeclampsia
- Favorable prognosis:
  - Decreased disease activity prior to conception
  - Normal renal function
  - Lack of antiphospholipid antibodies
- Often spontaneous remission in pregnancy
- Anti Ro (SSA) Ab associated with increased incidence of neonatal lupus and congenital heart block

SLE: TREATMENT

- Immunosupressives:
  - Glucocorticoids: Rx of choice
  - Azathioprine (Imuran)
  - Cyclophosphamide: Increased risk of infertility with duration of therapy, cumulative dose, and advancing age
  - Methotrexate: **X** Used to terminate ectopic pregnancies
- NSAIDs:
  - Premature closure of ductus arteriosus
  - Oligohydramnios due to fetal oliguria
- ASA: low dose for prophylaxis in APA

NEUROLOGIC DISORDERS

- Seizures
  - Increased incidence of congenital defects
  - Avoid valproic acid and trimethadione
  - monotherapy at lowest possible dose with folic acid supplementation
- Migraine Headaches
  - Acetaminophen
  - Avoid ergot alkaloids **X** cause fetal demise

INFECTIOUS DISEASE

- UTI
  - Treat asymptomatic (1/3 develop pyelo)
  - Usually E coli or Group B Strep
  - Amox, ceph
- Gonorrhea: more likely to disseminate
- Syphilis: Often asymptomatic
- Tuberculosis
  - INH, Ethambutol, Rifampin, and Pyridoxine
  - PPD+ chemoprophylaxis deferred until after delivery unless high risk

MOST TERATOGENIC VIRUSES

- Toxoplasmosis
  - Avoid raw meat, cat feces, garden soil
- Rubella
  - Congenital cardiac defects
- CMV
- HSV
- Varicella Zoster

HIV IN PREGNANCY

- Decreased vertical transmission 25.5% to 8.3% with zidovudine (New England Journal, 1994)
- Start after organogenesis
- Triple drug therapy controversial

CONCLUSION

- Increased incidence of chronic disease in pregnancy due to advanced maternal age
- Remember preconception counseling as organogenesis occurs before many women know they are pregnant
- In general, potential risks of pharmacologic agents outweigh risks of untreated illness

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